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Asian Pacific Journal of Tropical Biomedicine

journal homepage: www.elsevier.com/locate/apjtb

Epidemiological investigation http://dx.doi.org/10.1016/j.apjtb.2015.02.004

# Epidemiology of extra pulmonary tuberculosis in Eastern Sudan

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ARTICLE INFO

*Article history:*
Received 14 Jan 2015
Received in revised form 19 Jan 2015
Accepted 22 Feb 2015
Available online 27 May 2015

*Keywords:*
Extra pulmonary
Tuberculosis
Epidemiology
Sudan

ABSTRACT

**Objective:** To investigate the epidemiological factors associated with extra pulmonary tuberculosis (EPTB) in Kassala, Eastern Sudan.

**Methods:** Patients infected with TB (pulmonary and extra-pulmonary) documented at the hospital were interviewed with a structured questionnaire used to gather socio-demographic information. The diagnosis of EPTB cases was based on presence of tuberculous granulomas in the histological samples, positive PCR to DNA of myco-bacterium tuberculosis, radiological findings and fluid analysis suggestive of EPTB and clinical diagnosis with adequate response to anti-tuberculous therapy.

**Results:** A total of 985 patients with TB were enrolled in the study, including 761 (77.3%) with PTB and 224 (22.7%) with EPTB. The mean age (SD) of patients with PTB and EPTB was 33.2 (15.4) and 34.7 (14.6) years respectively. The prevalence of EPTB was at (22.7%), with TB lymphadenitis 79 (35.3%), marking the frequent form of EPTB followed by peritoneal TB 27 (12.05%). While residence and occupation were not associated with EPTB, those with lower level of education (OR = 0.3; confidence intervals (*CI*) = 0.2–0.5; $P < 0.001$), female (OR = 8.7, *CI* = 4.9–15.1, $P < 0.001$), non vaccination (OR = 70.3, *CI* = 34.2–144.3, $P < 0.001$), and non smoker (OR = 0.1; *CI* = 0.06–0.20; $P < 0.001$), were associated with high prevalence of EPTB.

**Conclusions:** Around one quarter of patients with TB in this study were more likely to have EPTB. Therefore, effective strategic plans regarding diagnostic procedures and control measures are needed to reduce the burden of the disease in Sudan.

## 1. Introduction

Tuberculosis (TB) is a major health problem worldwide. It has been estimated that there are eight million disease episodes and three million deaths each year [1], with underdeveloped countries accounting for 95% of reported TB nationwide cases [2]. The global estimate of extra pulmonary TB (EPTB) ranges from 17% to 52% of all cases of TB [3]. Although the number of TB cases has significantly decreased, the proportions of EPTB cases remained constant. Furthermore, EPTB accounts for 21% and 50% of total TB cases and HIV positive cases respectively [4,5]. Sudan has high prevalence of TB with the incidence rate of 114 cases per 100 000 of the population cases during 2012 [6]. The country accounts for 15% of the TB burden in the World Health Organization Eastern Mediterranean Region [7]. We recently observed that 26.6%

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Peer review under responsibility of Hainan Medical University.

of patients with TB in the same study area had EPTB [8]. In spite of this, there is little published data regarding EPTB [9]. Investigating the incidence rate and the factors associated with the occurrence of EPTB is fundamental to provide care givers and health planners with the basic data necessary for the preventive and treatment measures. Hence, the present study aimed to investigate the epidemiological factors associated with EPTB in Kassala, Eastern Sudan.

## 2. Materials and methods

This was a cross-sectional hospital-based study conducted at Kassala Teaching Hospital in Eastern Sudan between January 2011 and June 2012 to investigate the epidemiological factors of EPTB in Kassala Town of Eastern Sudan. Kassala was located nearly 600 km from Khartoum, the capital city, covering an area of 42 282 $km^2$ inhabited by 1.8 million people. Kassala Teaching Hospital was a tertiary hospital which provided services for all patients referred from health centers and rural hospitals. After singing an informed consent, all patients infected with TB (pulmonary and extra-pulmonary) documented at the hospital were interviewed with a structured questionnaire used to gather socio-demographic information (age, sex, education, residence, employment, history of contact with TB patients and vaccination with Bacillus Chalmette-Guerin). Cases of EPTB were defined according to the criteria set by the World Health Organization [10] by presence of TB outside the lung such as pleura, lymph nodes, abdomen, genitourinary tract, pericardium, meningitis, skin, joints and bones. The diagnosis of EPTB cases was based on presence of tuberculous granulomas in the histological samples, positive PCR to DNA of mycobacterium tuberculosis, radiological findings and fluid analysis suggestive of EPTB and clinical diagnosis with adequate response to anti-tuberculous therapy. Those patients were followed up for two months during the intensive phase. Smear for alcohol acid fast bacilli and chest radiograph were performed for all patients with PTB and for patients with miliary TB while tuberculin skin test and culture were not available in the study area. Cases with concurrent PTB-EPTB were excluded from the study. All TB patients were offered free TB medical care including diagnosis (for alcohol acid fast bacilli) and treatment as per the National Tuberculosis Control Program guidelines for Sudan, and had an access to treatment and follow up in the TB referral clinic which was open twice per week from 8:00 a.m. to 3:00 p.m.

### 2.1. Statistical analysis

Data was entered into a computer database and double-checked before analysis. SPSS software (SPSS Inc., Chicago, IL, USA, version 16.0) was used. Means and proportions for the socio-demographic characteristics were compared between the groups of the study using *t* and *Chi*-square tests, respectively. Univariate and multivariate analyses were performed. EPTB was the dependent variable and the socio-demographic characteristics were independent variables. Confidence intervals (*CI*) of 95% were calculated and $P < 0.05$ was considered significant. In case of discrepancy between the results of *t* and *Chi*-square tests and the results of multivariate analyses, the latter was taken as final.

### 2.2. Ethical approval

This study received ethical approval from the Research Committee at the Ministry of Health of Kassala State.

## 3. Results

### 3.1. Patients' characteristics

During the study period, a total of 985 patients diagnosed with TB (pulmonary and extra pulmonary) were recruited in this study. Of the 985 TB patients, PTB was found in 761 patients (77.3%). The mean age (SD) of patients with PTB and EPTB were 33.2 (15.4) and 34.7 (14.6) years respectively. The majority of these patients were male [612 (62.1%)], illiterates [528 (53.6%)], rural residents [652 (66.2%)] and unemployed [422 (42.8%)] (Table 1). Cough was found in 805 (81.7%), fever in 961 (97.5%), weight loss in 774 (78.5%), and contact with patient with TB was found in 591 (60%) patients.

**Table 1**
Demographic characteristic(s) of TB patients in Kassala, Eastern Sudan.

| Variable | Total TB patients ($N$ = 985) | PTB patients ($N$ = 761) | EPTB patients ($N$ = 224) | $P$ |
|---|---|---|---|---|
| Age ≤30 years | 474 (48.2%) | 345 (45.4%) | 129 (57.6%) | <0.001 |
| Gender: Female | 373 (37.9%) | 192 (25.2%) | 181 (80.8%) | <0.001 |
| Rural residence | 652 (66.2%) | 485 (63.7%) | 167 (74.6%) | 0.003 |
| Illiterate | 528 (53.6%) | 375 (49.3%) | 153 (68.3%) | <0.001 |
| Non employees | 422 (42.8%) | 331 (43.6%) | 91 (43.6%) | 0.241 |
| Non vaccination | 372 (37.8%) | 160 (21.0%) | 212 (94.6%) | <0.001 |
| Nonsmoker | 447 (45.4%) | 253 (34.0%) | 194 (86.6%) | <0.001 |

### 3.2. EPTB involvement

EPTB was detected in 224 (22.7%) patients, of these TB lymphadenitis was the predominant manifestation [79 (35.3%)], followed by TB peritonitis in 27 (12.05%) patients, female genital TB in 25 (11.2%), tubercular pleural effusion in 15 (6.7%) and military TB in 15 (6.7%) (Figure 1).

### 3.3. Diagnosis of EPTB

The diagnosis of extra pulmonary was confirmed by the presence of tuberculous granulomas in histological samples in 102 (45.54%) patients, by positive PCR for *Mycobacterium tuberculosis* DNA in 43 (19.20%) patients, by clinical diagnosis and adequate response to anti-tuberculous therapy in 60 (26.79%) patients, by presence of miliary nodules in chest radiographs in 11 (4.9%) patients, and by spinal magnetic resonance imaging and cerebrospinal fluid analysis in 8 (3.57%) patients with Pott's disease of the spine. In the logistic regression model, while residence and occupation were not associated with EPTB, lower level of education (OR = 0.3; $CI$ = 0.2–0.5; $P < 0.001$), female (OR = 8.7, $CI$ = 4.9–15.1, $P < 0.001$), non vaccination (OR = 70.3, $CI$ = 34.2–144.3, $P < 0.001$), and nonsmoker (OR = 0.1; $CI$ = 0.06–0.20; $P < 0.001$), were associated with high prevalence rate of EPTB (Table 2).

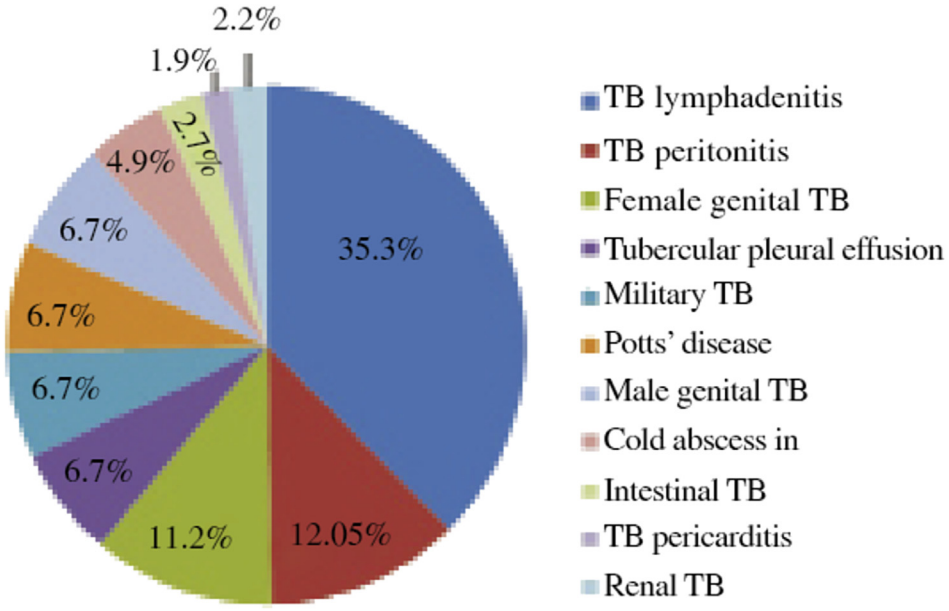


**Figure 1.** Site of extra-pulmonary TB involvement.

**Table 2**

Factors associated with EPTB in Kassala, Eastern Sudan according to univariate and multivariate analysis.

| Variable | Univariate analysis | | | Multivariate analysis | | |
|---|---|---|---|---|---|---|
| | OR | 95% *CI* | *P* | OR | 95% *CI* | *P* |
| Age <33.4 years | 1.02 | 1.01–1.03 | <0.001 | 0.3 | 1.00–1.03 | 0.053 |
| Female gender | 12.50 | 12.50–18.00 | <0.001 | 8.7 | 4.90–15.10 | <0.001 |
| Rural residency | 0.60 | 0.40–0.40 | 0.003 | 0.9 | 0.50–1.80 | 0.836 |
| Illiterate | 0.50 | 0.40–0.70 | <0.001 | 0.3 | 0.20–0.50 | <0.001 |
| Unemployed | 1.10 | 0.90–1.30 | 0.143 | 1.2 | 0.90–1.50 | 0.238 |
| Non vaccination | 66.40 | 36.20–121.80 | <0.001 | 70.3 | 34.20–144.30 | <0.001 |
| Nonsmoker | 0.08 | 0.05–0.10 | <0.001 | 0.1 | 0.06–0.20 | <0.001 |

## 4. Discussion

EPTB is a significant public health problem that represents a diagnostic challenge in Eastern Sudan. The current study demonstrated high prevalence of EPTB in an area with high incidence of TB, which is true for those with lower level of education, female gender, young patients, unvaccinated and nonsmokers. The proportion of EPTB in our study was estimated at 22.7%, which is similar to that reported in countries such as the US (21.0%), Japan (23.0%), Cameroon (26.6%), India (19.0%) and Pakistan (18.0%). However, the proportion of EPTB in the present study is lower than that of the other developed countries such as Italy (32%) and Australia (39%) [11,12]. These differences may be attributed to differences in socio-demographic characteristics or due to failure of early recognition and under-estimation of EPTB in developing countries like Sudan because of lack of facilities to diagnose EPTB in these settings. More than one quarter of extra pulmonary cases in our study were therefore diagnosed by clinical response to anti TB therapy.

The most frequent form of EPTB was TB lymphadenitis followed by TB peritonitis. This was in accordance with retrospective analysis of TB patients from Nepal, which showed that the lymph nodes were the most common EPTB sites involved, followed by abdominal TB. Lymphatic TB predominates is the most frequent type of EPTB in areas with low incidence of tuberculosis [4,13–15]. Studies conducted in other countries showed TB lymphadenitis as the common form of EPTB followed by pleural TB [16,17]. In contrast, many other reports have shown pleural effusion as the most frequent form of EPTB, followed by lymphatic TB [18,19]. The reasons for these discrepancies were unknown; however, many authors considered pleural TB as an early manifestations of primary mycobacterial infection [20]. Among socio-demographic factors and in agreement with other reports [4,13,21,22], we found that female was significantly associated with EPTB, which can be explained by socio-cultural factors such as illiteracy, short birth interval, house work, early marriage. All these factors might suppress the females' immunity and increase susceptibility to infection with TB. We also found in this study that younger age was an independent risk factor for EPTB. This is in line with studies from developed and developing countries where reports have significantly associated EPTB with younger age [13,23].

The association between lower level of education and EPTB found in the present study disagreed with the results obtained in Brazil where EPTB was strongly associated with higher level of education [19]. Previously, we reported illiteracy as the predictor of PTB [8]. Furthermore, many other studies confirmed low level of education as social determinants for EPTB [23,24], which might be related to the fact that education might improve the standard of living, increase the awareness of health problem and encourage the seeking for medical care.

Our results also demonstrated that smoking was not associated with EPTB. This is consistent with other studies which reported smoking as the risk factors for PTB than EPTB [25,26]. Moreover, smoking has been proved to be associated with both relapse of TB and TB mortality. Smoking increased the risk of TB by the following means: reducing alveolar macrophage activity, immune suppression of pulmonary lymphocytes and reduction of cytotoxic activity of natural killer cells [27,28]. As observed in another study, history of non vaccination was significantly associated with EPTB [21]. Increased public awareness of TB in general and extra pulmonary TB in particular is essential to reducing the burden of the disease.

Our study has a few limitations. Firstly, being conducted in hospital might not reflect reality of the community. Secondly, some of the populations examined were clinically diagnosed by response to anti-tuberculosis. Finally, the present study did not investigate the HIV serology. This is quite important to be performed, since HIV is common among TB patients.

The result of this study demonstrated that EPTB is more common among females, young patients and illiterates. Knowledge of demographic characteristics of cases of EPTB, and improvement of diagnostic facilities are essential for early recognition and better treatment of EPTB cases.

## Conflict of interest statement

We declare that we have no conflict of interest.

## Acknowledgments

We are grateful to all those who participated in this study, namely, the staff of Kassala Teaching Hospital.

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